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EXAMINER

BRUMBACK, B

ART UNIT

PAPER NUMBER

1643

II

DATE MAILED: 10/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No. <b>09/005,034</b>	Applicant(s) <b>Brenda Brumback</b>	Law <b>Group Art Unit 1643</b>

Responsive to communication(s) filed on Jun 9, 1999

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 20-25 and 27-32 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 20-25 and 27-32 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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## **DETAILED ACTION**

1. The amendment filed 06/09/99 has been received and made of record as Paper #10. Claim 26 was canceled. Claim 20 was amended. New claims 28-32 were added. Pending claims are 20-25 and 27-32.

### ***Claim Rejections - 35 USC § 112***

3. All rejections of claims 20-27 under 35 U.S.C. 112, second paragraph, are withdrawn subsequent to applicant's claim amendments and arguments of 6/09/99, which were persuasive.

4. The rejection of claim 20 under 35 U.S.C. 112, first paragraph, for recitation of proliferating myogenic cells is withdrawn pursuant to applicant's claim amendment of 06/09/99. The rejection of claim 26 for recitation of proliferated MHC-1 deficient fat cells is moot, as claim 26 has been canceled.

5. The remaining rejections of claims 20-25 and 27 under 35 U.S.C. 112, first paragraph, are maintained. Additionally, newly added claims 28-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the original reasons of record for claims 20-27 and for the

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additional reasons outlined below. Applicant's arguments have been fully considered but they are not persuasive for the following reasons.

Applicant argues that the specification provides guidance for cell therapy in humans from the bottom of page 24 through page 25 and on page 26, lines 9-10. This is not found to be persuasive because the portions of the specification referenced by applicant describe methods for myoblast injection "into the gastrocnemius muscles of twenty normal 3-month old normal **mice**", not humans (emphasis added; see page 25, lines 13-14). It is therefore unclear how this portion of the disclosure can be said to enable treatment in humans.

Applicant argues that "...the inventor believes that transplantation in a larger human muscle or body part actually provides superior results in comparison to the mouse model because the mouse muscle is too small to get real transverse injection". Firstly, this statement is difficult to reconcile with the referenced teachings of successful transverse injection in mice which are found on page 25. Secondly, absent any supporting evidence, such a statement based solely on a belief is insufficient to overcome the teachings found in the art and pointed out in the previous Office action (Paper # 6), *i.e.* that human transfer has not been successful and is at best controversial (see page 4, paragraph b.).

Applicant argues that the fact that the specification teaches that "myofiber orientation of different muscle groups have to be well studied by the orthopedic surgeons who administer myoblast injections" ... "allows for greater success in the human than in the mouse". However, applicant has provided no reasoning why this would be so. In fact, the referenced portion of the

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specification would seem to point more toward increased unpredictability in humans because it teaches that human muscles are larger than mouse muscles and the myofiber orientation of different muscles in humans has to be studied prior to injection.

Applicant makes a general statement that the inventor injects more than 10 billion cells with 200 transverse injections, while "in contrast, others who had failed typically have injected only a total of about 600 million cells over 200 injections, of unknown orientation". Firstly, the basis for applicants assertion is not clear, since no references describing these experiments were provided. Secondly, no data correlating cell numbers inoculated with any alteration in cosmetic appearance (as is claimed) has been provided. Thirdly, the portion of the specification referenced by applicant pertains to injection of myoblasts into a number of different muscles in boys with Duchenne muscular dystrophy (DMD) or infantile facioscapulohumeral dystrophy (IFSH). Applicants claims are not limited to those conditions, but encompass cosmetic alteration of nondiseased body parts.

The relevance of applicant's statements pertaining to "various injection methods", the necessity "to inject as pure as possible a fraction", the transfer medium , and exercise and physical therapy, is not understood, as these statements do not appear to pertain to any points of the outstanding rejection.

Applicant's statements regarding Appendix B are noted; however, this information could not be considered, as no appendix B was found attached to the amendment filed 06/09/99.

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The relevance of applicant's statement that "a skilled artisan can find muscle in breast tissue and in a hip" is not clear (see paper # 6, pages 4-5, paragraph 4c.). The art teaches that (in mice) myoblasts contribute to the formation of new muscle *in vivo* by fusing with endogenous myoblasts and that myoblasts only fuse with myoblasts. Is applicant's statement made in order to overcome or circumvent these teachings? Applicant also states that the present invention does not rely on fusion of myoblasts with adipocytes. If this is so, then how does the injection of myoblasts effect a cosmetic alteration, given the teachings in the art that cell fusion is the process by which myoblasts increase muscle mass?

In response to applicant's assertion that the applicant has provided teachings necessary to overcome conventional wisdom, the examiner maintains that no such teachings have been provided. Arguments in the absence of evidence are not persuasive.

Applicant's statements regarding the 1992 DiMaro publication are not completely understood; however, it would seem that applicant is stating the DiMaro is not relevant because "because the claimed method for augmentation of soft tissue injures the muscle" due to injection. DiMaro describes myogenic cell transfer. Such cells are transferred by injection. Therefore, DiMaro would seem to be relevant. Furthermore, applicant's proceeding statement regarding minimization of injury from injection would seem to contradict the first statement, which suggests that the injury is somehow relevant to the claimed method of effecting a cosmetic alteration.

Applicant argues that Morgan et al. is not relevant to the claimed invention because immunocompromised animals were used, whereas in the present invention non-immune

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compromised humans are used. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., nonimmunocompromised hosts) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Morgan et al. teach injection of immunosuppressed animals to avoid graft vs. host disease. Applicant's argument, therefore, raises an additional issue of enablement as to how such a reaction is to be avoided in the claimed method, wherein immunocompetent individuals are injected with cultured allogeneic myogenic cells.

The examiner notes applicant's referral to the portion of the specification wherein it is stated that the problem of tumor production can be avoided by limiting the proliferation to no more than 30 generations; however, this single statement, absent any supporting evidence, is not sufficient to overcome the rejection, in light of the teachings in the art. The art teaches that "passage number" denotes the number of times a cell line is subcultured or "split" *in vitro* prior to inoculation into the host. Morgan teaches that tumor formation results from further proliferation of the implanted cells after injection. Thus, absent any supporting evidence, the passage number of the injected cells prior to injection would not seem to be the critical factor for tumor formation and applicant's argument is thus not persuasive.

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***Claim Rejections - 35 USC § 112/Additional Grounds of Rejection***

6. Claims 31 and 32 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reciting dissection as a method for augmenting a body part. The instant claims recite a method for augmenting a body part comprising dissecting and removing tissue from the body part and surgically implanting myotubes into the body part. The art teaches that surgical procedures are performed so as to minimize trauma to the patient; therefore, the art teaches that surgical implants are performed without dissecting the body part from the individual. Given these general teachings, it is difficult to reconcile dissection as a viable means of augmenting a body part. Additionally, absent any step of reinsertion of the body part, one of skill in the art would be unable to practice the invention as claimed.

7. Claims 31 and 32 are also rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is reinsertion of the body part after dissection.

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***Double Patenting***

8. The examiner notes applicant's intention to file a terminal disclaimer in the event that claims conflicting with claims 5-11 of copending Application No. 09/005,035 are allowed. This rejection is held in abeyance until such time.

***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Lynette

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Smith whose telephone number is (703) 308-3909. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1643 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1643 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback  
October 5, 1999



DONNA WORTMAN  
PRIMARY EXAMINER